REMARKS

Claims 1-20, 27 and 28 are canceled without prejudice or disclaimer and claims 21 and 22 are amended. The currently pending claims are 21-26 and 29-53.

The specification is amended to add a cross reference to the prior application and correct typographical errors in the specification.

Applicants respectfully request that the Preliminary Amendment described herein be entered into the record prior to examination and consideration of the above-identified divisional application.

If the Examiner wishes to discuss any issues concerning this communication by telephone, please contact the below-signed attorney at (612) 305-1217.

If any additional fees are deemed necessary in this instance, please charge Deposit Account No. 13-4895.

CERTIFICATE UNDER 37 C.F.R. 1.10:

Express Mail label number EL776900604US
Date of Deposit March 20 2001

I hereby certify that this paper and/or fee is/are being deposited with the United States Postal Service Express Mail Post Office to Addressee service under 37 C.F.R. 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Attn: Box PATENT APPLICATION, Washington, D. C. 20231.

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March 20, 2001
Date

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APPENDIX A: Specification/Claim Amendments Including Notations to Indicate Changes Made

Title:	**PEPTIDE ANTAGONISTS OF CGRP-RECEPTOR SUPERFAMILY AND METHODS OF USE**
Applicant:	Derek D. Smith et al.
Serial No.:	unknown (parent: 09/070,504)
Filed:	herewith

In the Specification

The following new paragraph has been inserted at page 1, line 4:

Continuing Data

This is a divisional application of Serial No. 09/070,504, filed April 30, 1998 (pending), which is incorporated herein by reference.

The paragraph beginning at page 1, line 11, has been amended as follows:

The calcitonin gene related peptide (CGRP) is a sensory neuropeptide with potent vasodilatory and cardiotonic action as described in U.S. Pat. No. 4,530,838 to Evans et al. The peptide exists in two forms (denoted α and β). α-CGRP is produced by the calcitonin gene (Amara et al. *Nature* 298:240-244, 1982 and Rosenfeld et al. *Nature* 304:129-135, 1983) while β-CGRP is the product of a separate gene (Amara et al. *Nature* 298:240-244, 1985 and Steenbergh et al. *FEBS Lett.* 183:403-407,**[1985]** **1982**). The human β-form and α-form differ by three amino acids.

The paragraph beginning at page 1, line 27, has been amended as follows:

The release of CGRP from sensory nerve endings in inflammatory reactions can result in the local acceleration of microhemodynamic changes including vasodilation and permeability of the microcirculation resulting in plasma exudation and the release of humoral factors and inflammatory cells to the site of injury. CGRP has been used as a vasodilator in animal models of subarachnoid hemorrhage and in trials involving human subjects with congestive heart failure. CGRP administration produced hypotension associated with moderate tachycardia in hypertensive humans (Jian et al. *Chin. Med. J.* 102:897-901, 1989). CGRP has also been used as a potent dilator of the coronary circulation (Ezra et al., *Eur. J. Pharmacol.*, 1987). In contrast to

nitrates, which have also been used as vasodilators, CGRP results in dilation by both endothelium-dependent and endothelium-independent mechanisms. Also, in contrast to nitrates, such as sodium nitroprusside, tolerance to CGRP has not been noted (**[Foulkes]** **Bény** et al. *Regul. Pept.* 25:25-36, 1989). CGRP has been demonstrated to improve the ability of patients to participate in exercise programs in patients with chronic stable angina (Uren et al. *Cardiovasc. Res.* 27:1477-1481, 1993).

The paragraph beginning at page 3, line 27, has been amended as follows:

CGRP antagonists includes peptides from CGRP including amino acids 8-37 of β- CGRP (**[Chiba]** **Park** et al. *Am. J. Physiol.* 1989) having the amino acid sequence: THRLAGLLSRSGGMVKSNFVPTNVGSKAF (SEQ ID NO:1) and peptides from α-CGRP including amino acids 8-37 and having the amino acid sequence THRLAGLLSRSGGMVKSNFVVPTNVGSKAF. β-CGRP(8-37) (SEQ ID NO:2) has been used to counteract the effects of CGRP. For example, CGRP(8-37) has been shown to reverse the hypotension and tachycardia produced by administration of LPS to rats (Huttemeir, et al. *Am. J. Physiol.* 265:H767-H769, 1993). In addition, CGRP(8-37) has some activity against amylin (Gardiner et al. Diabetes 40:948-951, 1991). The affinity for CGRP(8-37) varies between tissues. For example, data indicates that the affinity of CGRP(8-37) for mesenteric artery, kidney, heart and skeletal muscle is somewhat higher than the affinity of CGRP(8-37) for adipocytes and descending colon (Poyner, D. *Trends in Pharm. Sci.* 16:424-428, 1995).

APPENDIX A: Specification/Claim Amendments Including Notations to Indicate Changes Made

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The paragraph beginning at page 10, line 15, has been amended as follows:

Preferred adrenomedullin-derived antagonists include:

h-adrenomedullin (22-52) (SEQ ID NO:23)

(TVQKLAHQIYQFTDKDKDNVAPRSKISPQGY-NH_2 [Watanabe,] Eguchi et al. [Endocrinol.] *Endocrinol.* 135:2454-2458, 1994 and Champion et al. *Am. J. Physiol.* 272:R234-242, 1997)[,] .

In the Claims

21. (AMENDED) The method of Claim [20] 29 wherein the CGRP receptor is on a cell.

22. (AMENDED) The method of Claim [20] 29 wherein the CGRP receptor is cell free.